

**WHAT IS CLAIMED IS:**

1. A method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of at least one copolymer 1 or copolymer 1-related heteropolymer in combination with at least one immunosuppressive drug, said copolymer 1 or copolymer 1-related heteropolymer comprises at least three amino acids each one selected from at least three of the following groups:

- (a) lysine and arginine;
- (b) glutamic acid and aspartic acid;
- (c) alanine, glycine and valine;
- (d) tyrosine, tryptophan and phenylalanine.

2. The method of claim 1, wherein said copolymer 1 or copolymer 1-related heteropolymer is selected from the group consisting of a random heteropolymer, an ordered heteropolymer, or an ordered peptide.

3. The method of claim 2, wherein said ordered peptide is selected from SEQ ID NOS: 1-32.

4. The method of claim 1, wherein said immunosuppressive drug is selected from the group consisting of antiproliferative drugs, inhibitors of lymphocyte activation, steroids, purine antimetabolites, antibodies and immunomodulators.

5. The method of claim 4, wherein said immunosuppressive drug is cyclosporin A, FK 506, ISA247, FK 778, rapamycin, everolimus or FTY720.

6. The method of claim 1, wherein said graft rejection is associated with transplantation of cells, tissue or organs, selected from hematopoietic cells, stem cells, heart, lung, kidney, liver or skin.

7. The method of claim 1, wherein said therapeutically effective amounts of copolymer 1 or copolymer 1-related heteropolymer and said at least one immunosuppressive drug are administered together or sequentially.

8. The method of claim 2, wherein said copolymer contains four different amino acids each one selected from the groups (a) to (d).

5 9. The method of claim 8, wherein said heteropolymer comprises in combination alanine, glutamic acid, lysine, and tyrosine, of net overall positive electrical charge and of a molecular weight of about 2,000 to about 40,000 daltons.

10 10. The method of claim 9, wherein said heteropolymer has a molecular weight of about 2,000 to about 13,000 daltons.

11. The method of claim 2, wherein said heteropolymer contains three different amino acids each one selected from the groups (a) to (d), herein referred to as terpolymer.

15 12. The method of claim 11, wherein said terpolymer consists essentially of the amino acids tyrosine, alanine and lysine.

20 13. The method of claim 12, wherein said terpolymer consists essentially of tyrosine, alanine and lysine, in the molar ratio of from about 0.005 to about 0.25 tyrosine, from about 0.3 to about 0.6 alanine, and from about 0.1 to about 0.5 lysine, herein designated YAK.

25 14. The method of claim 11, wherein said terpolymer consists essentially of the amino acids glutamic acid, tyrosine and lysine.

30 15. The method of claim 14, wherein said terpolymer consists essentially of the amino acids glutamic acid, tyrosine, and lysine in the molar ratio of from about 0.005 to about 0.300 glutamic acid, from about 0.005 to about 0.250 tyrosine, and from about 0.3 to about 0.7 lysine, herein designated YEK.

16. The method of claim 11, wherein said terpolymer consists essentially of the amino acids tyrosine, glutamic acid, and alanine.

17. The method of claim 16, wherein said terpolymer consists essentially of the amino acids tyrosine, glutamic acid, and alanine in the molar ratio of from about 0.005 to about 0.25 tyrosine, from about 0.005 to about 0.3 glutamic acid, and from about 0.005 to about 0.8 alanine, herein designated YEA.

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18. The method according to claim 2, wherein the amino acids comprising the heteropolymer are all L-, all D- or a mixture of L- and D-amino acids.

19. A pharmaceutical composition for use in preventing and treating graft rejection, comprising a therapeutically effective amount of at least one synthetic peptide copolymer selected from glatiramer acetate and a copolymer 1-related heteropolymer according to claim 1 in combination with at least one immunosuppressive drug and a pharmaceutically acceptable carrier.

20. The pharmaceutical composition of claim 19 in unit dosage form suitable for oral administration.

21. The pharmaceutical composition of claim 19 in unit dosage form suitable for parenteral injection.

22. A method of treating or preventing graft rejection in a subject in need thereof, comprising administering a therapeutically effective amount of at least one ordered peptide or ordered copolymer 1-related heteropolymer, said ordered peptide or ordered copolymer 1-related heteropolymer comprising at least three amino acids each one selected from at least three of the following groups:

- (a) lysine and arginine;
- (b) glutamic acid and aspartic acid;
- (c) alanine, glycine and valine;
- (d) tyrosine, tryptophan and phenylalanine.

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23. The method of claim 22, wherein said copolymer contains four different amino acids each one selected from the groups (a) to (d).

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24. The method of claim 22, wherein said heteropolymer contains in combination alanine, glutamic acid, lysine, and tyrosine, of net overall positive electrical charge and of a molecular weight of about 2,000 to about 40,000 daltons.

25. The method of claim 24, wherein said heteropolymer has a molecular weight of about 2,000 to about 20,000 daltons.

5        26. The method of claim 22, wherein said heteropolymer contains three different amino acids each one selected from the groups (a) to (d), herein referred to as terpolymer.

10        27. The method of claim 26, wherein said terpolymer consists essentially of the amino acids tyrosine, alanine and lysine.

15        28. The method of claim 27, wherein said terpolymer consists essentially of tyrosine, alanine and lysine, in the molar ratio of from about 0.005 to about 0.25 tyrosine, from about 0.3 to about 0.6 alanine, and from about 0.1 to about 0.5 lysine, herein designated YAK.

29. The method of claim 26, wherein said terpolymer consists essentially of the amino acids glutamic acid, tyrosine and lysine.

20        30. The method of claim 29, wherein said terpolymer consists essentially of the amino acids glutamic acid, tyrosine, and lysine in the molar ratio of from about 0.005 to about 0.300 glutamic acid, from about 0.005 to about 0.250 tyrosine, and from about 0.3 to about 0.7 lysine, herein designated YEK.

25        31. The method of claim 26, wherein said terpolymer consists essentially of the amino acids tyrosine, glutamic acid, and alanine.

30        32. The method of claim 31, wherein said terpolymer consists essentially of the amino acids tyrosine, glutamic acid, and alanine in the molar ratio of from about 0.005 to about 0.25 tyrosine, from about 0.005 to about 0.3 glutamic acid, and from about 0.005 to about 0.8 alanine, herein designated YEA.

33. The method of claim 22, wherein the amino acids comprising the heteropolymer are all L-, all D- or a mixture of L- and D-amino acids.

5 34. The method of claim 22, wherein said ordered peptide is selected from SEQ ID NOS: 1-32.

35. The method of claim 22, wherein said ordered copolymer is an oligomer of at least one ordered peptide selected from SEQ ID NOS: 1-32.

10 36. The method of claim 22, wherein said graft rejection responses are associated with transplantation of cells, tissues or organs selected from hematopoietic cells, stem cells, heart, lung, kidney, liver and skin.

15 37. The method of claim 36, wherein said organs are HLA-matched or HLA-unmatched.

38. The method of claim 36 wherein the cells are HLA-matched or HLA-mismatched.

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